ISSN 2959-409X

Gamma wave frequency affect Microglial states

Jiabao Shen

Beijing Haidian Kaiwen Academy, Beijing, 100195, China
20200801001@hd.kaiwenacademy.cn

Abstract:

Alzheimer's disease (AD) is a chronic neurodegenerative disease, and its core symptoms are memory loss and cognitive impairment. Recent studies show that gamma wave oscillation plays an important role in regulating the protein level of starch and slowing down the progress of AD. This study focuses on the effect of gamma wave oscillation on the formation of amyloid spots in AD mouse model, and evaluates its possibility as a non-invasive treatment.

Keywords: Alzheimer's disease; Gamma wave oscillation; Non-invasive treatment of amyloid; Degenerative diseases of nervous system.

1. Introduction

Alzheimer's disease (AD) is a chronic neurodegenerative disease with the main symptoms of memory loss and cognitive dysfunction. The widely accepted etiological explanation of AD is the formation of amyloid (A) plaques in the brain, which is considered as a key factor in the development of the disease. However, the specific mechanism of these stains leading to neurodegeneration still needs further study [1]. Recently, researchers have proposed that gamma wave oscillation, a brain electrical activity model that can regulate A level and slow down the development of AD, plays an important role.

The fluctuation of frequency from 30 Hz to 100 Hz is very important for attention, memory, recognition and other cognitive functions. Abnormal gamma wave activity was observed in some nervous system diseases, including AD. It is worth noting that the change of gamma wave rhythm is related to the change of synaptic function and communication between neurons, which may affect the accumulation of neurotoxic proteins (such as A). Hannah F. Iaccarino and his team's research results show that: "Especially at the frequency of 40Hz, the content of Amyloid β(ATA) can be reduced, and the pathological changes related to AD can be reduced." [2] [3]This shows that gamma wave oscillation is a symbol of disease progress and may also become a potential target of treatment.

The current research aims to explore the effect of plutonium oscillation on the formation of amyloid plaques in AD mouse model. In this study, optogenetics technique was used to induce Gamma Zhen Tang with a specific frequency as a non-invasive treatment for AD, and the potential of Gamma Zhen Tang was evaluated [4]. A deep understanding of the relationship between peptide activity and A pathology is expected to provide valuable clues for formulating new treatment strategies and strengthen our understanding of the pathogenesis of AD.

2. Hypothesis

In this study, the hypothesis that the expression of BACE1 and the content of amyloid β protein were reduced by 40Hz gamma wave stimulation was put forward, and at the same time, colloidal cells changed from M1-type state which promoted inflammation to M2-type state which was anti-inflammatory. This process is expected to improve the cognitive function of APP/PS1 mouse.

3. Method

3.1 Step 1: Animal Model and Grouping

In this study, we selected genetically modified APP/PS1 mice (recognized research model of Alzheimer's disease) and wild-type (WT) mice as control groups to explore the effects of gamma wave stimulation on glial cell activity and cognitive ability. The experimental setup is divided into four groups: WT control group without gamma wave stimulation, WT group with gamma wave stimulation, APP/PS1 control group without gamma wave stimulation, and APP/PS1 group with gamma wave stimulation. Each team will receive 4 weeks of treatment and evaluation. Among them, the mice stimulated by gamma waves received 40 Hz gamma waves for one hour every day.

3.2 Step 2: Assessment Timepoints

Start criteria (before the start of stimulation), middle (two weeks) and end (four weeks). At each evaluation stage, a

series of detailed inspections will be carried out on rats.

3.3 Step 3: BACE1 Expression and Activity Analysis

Quantitative polymerase chain reaction (qPCR) blot (Western Blot were used to detect the expression and activity of BACE1. The analysis of enzyme activity will be used to evaluate the function of BACE1 in brain bacterial fluid. The specific operating procedures are as follows:

1. Collecting samples: Collect hippocampus and cortex tissue into freezing tubes for labeling and store them in the refrigerator at -80℃.

2.RNA extraction: RNA extraction kit, and configure total RNA extraction according to the operation guide.

3.cDNA synthesis: reverse transcription kit, which converts the extracted RNA into cDNA.

4. Based on the specific preinder sequence of the BACE1 gene, a group of highly selective premers are carefully designed and synthesised. Subsequently, the qCPR test kit is used to mix the cDNA template with these primers and perform real-time fluorescence quantitative polymerase chain reaction (qPCR) amplification. The cyclic parameters of the amplification process are set as: first, 3 minutes of pre-transformation processing at 95℃, then denature at 95℃ for 30 seconds, then annealing at 60℃ for 30 seconds, and extending at 72℃ for 30 seconds. This process undergoes 40 consecutive cycles.

5.Data analysis: The expression of BACE1 mRNA was quantitatively analyzed by observing the amplification curve and dissolution curve.

3.4 Step 4: Amyloid-beta Quantification

In order to deeply explore the pathological process of Alzheimer's disease, this study used enzyme-linked immunosorbent assay (ELISA) to quantitatively analyse the concentration of amyloid peptides in brain tissue samples, focussing on the concentration levels of ABA 40 and ABA 42. The abnormal accumulation of two main forms of amyloid peptide, A-40 and A-42, in the brain will lead to neuronal damage, loss and the formation of amyloid aggregates, which will lead to Alzheimer's disease.

3.5 Step 5: Microglial Activation State Assessment

The purpose of this study is to explore the activation state of bovine pontine cells by immunohistochemical method and identify specific markers related to M1 (inflammation-promoting) and M2 (inflammation-inhibiting) bovine pontine cells. In this way, we aim to evaluate whether gamma wave stimulation can induce cells to become anti-inflammatory The experimental design includes three groups: control group, γ wave stimulation group, γ wave stimulation group and immune tissue group, each group includes 10 mice.

In the gamma wave stimulation group, mice were exposed to gamma waves with specific frequency and intensity for 1 hour and 7 days every day. The mice in the control group will not be investigated by gamma wave. Immunohistochemical technique can judge the type and functional state of cells by detecting the expression of specific antigens in tissues or cells. In this experiment.

3.6 Step 6: Bahavioral Assessments

Objective To analyze the behavior of Morris water maze and Y maze experiment, and evaluate cognitive ability and memory. Through these experiments, we can explore the potential effect of gamma wave stimulation on cognitive decline treatment. The research design was divided into four groups: normal control group, model control group, simulated stimulation group and gamma wave stimulation group. The routine control group did not do any treatment and maintained its daily state. Animals in the model control group will use specific means to establish a model of cognitive degradation. Animals in the simulated stimulation group received the same treatment as those in the gamma wave stimulation group, but used ineffective stimulation. Animals in the gamma wave stimulation group will be stimulated by the actual gamma wave.

3.7 Step 7: Data Analysis

The collected data went through a rigorous statistical analysis process to explain the importance of the observation results, and to connect the changes among the indicators of BACE1 content, starch concentration, activation degree of glial cells and cognitive function. Through the preliminary explanation and statistical processing of the collected information (including the average calculation of each index, standard deviation, extreme value and other basic statistical indicators), we can know the distribution of the data.

4. Expected Results

The expected results of this study focus on the role of gamma wave in alleviating the pathology of Alzheimer's disease and improving cognitive ability. We estimate that 40Hz gamma irradiation will significantly reduce the expression and activity of BACE1 in the brain of APP/PS1 rats, which will lead to the decrease of amyloid peptide concentration, especially the important ABA 40 and ABA 42. This downward trend may come from the weakening of the cutting effect of BACE1 on APP.

At the same time, gamma wave stimulation is expected to affect the activation mode of glial cells, and promote them to change from M1 (inflammatory) state to M2 (anti-inflammatory) state, which can be verified by the expression

changes of immune tissue markers. This change implies the adjustment of neuroinflammatory environment, which is helpful to reduce the harmful inflammatory reaction related to Alzheimer's disease [5].

In addition, the transformation from M1 to M2 microglia highlights the role of neuroinflammation in Alzheimer's disease and the ability of gamma wave to regulate brain immune response. This change can not only reduce the harmful inflammatory reaction, but also promote neuroprotective activities, provide a better environment for the survival and synaptic function of neurons, and improve the cognitive ability against neurodegenerative diseases.

We also expect APP/PS1 mice stimulated by gamma waves to improve their cognitive expression in Morris water maze and Y maze tests to reflect better memory retention and spatial learning ability. These expected results will provide important clues for the potential of gamma wave stimulation as a non-invasive treatment to change the course of Alzheimer's disease and improve life expectancy of AD patients.

Experiments show that gamma wave stimulation can change bovine glial cells from M1 inflammatory state to M2 anti-inflammatory state, thus regulating the immune response in the brain. This regulation can be achieved by affecting the metabolism and signal transmission pathway of glial cells. The enhancement of M2 status is helpful to alleviate inflammatory reaction and promote the process of nerve protection and repair.

The results show that 40Hz gamma wave stimulation has obvious therapeutic prospects for pathological remission and cognitive function improvement of Alzheimer's disease. Gamma wave stimulation provides a potential non-invasive treatment strategy by reducing the expression and activity of BACE1, reducing the level of amyloid peptide, adjusting the phenotype of glial cells and improving cognitive function. Experiments show that gamma wave stimulation can directly affect the gene expression of BACE1, and can also reduce the activity by regulating other signaling pathways.

Nevertheless, the research still has the limitations of limited sample size and lack of in-depth discussion on the mechanism of gamma wave stimulation. Future research needs more samples and deeper mechanism analysis. It can verify the clinical application value of gamma wave stimulation in the treatment of Alzheimer's disease, and explore the possibility of different frequency and intensity of gamma waves on the disease. Through continuous research, we are expected to provide more effective treatment for Alzheimer's patients.

References

[1] Hsu, Chin-Hung, et al. "Ultrasound reduces inflammation by modulating M1/M2 polarization of microglia through STAT1/STAT6/PPARγ signaling pathways." CNS Neuroscience & Therapeutics 29.12 (2023): 4113-4123.

[2] Li, Long, et al. "Disease Stage-Associated Alterations in Learning and Memory through the Electroacupuncture Modulation of the Cortical Microglial M1/M2 Polarization in Mice with Alzheimer's Disease." Neural plasticity 2020.1 (2020): 8836173.

[3] Iaccarino, Hannah F., et al. "Gamma Frequency Entrainment Attenuates Amyloid Load and Modifies Microglia." Nature, vol. 540, no. 7632, 7 Dec. 2016, pp. 230–235, https://doi.org/10.1038/nature20587. Accessed 25 Sept. 2021.

[4] Park, Mincheol, et al. "Effects of transcranial ultrasound stimulation pulsed at 40 Hz on Aβ plaques and brain rhythms in 5× FAD mice." Translational Neurodegeneration 10 (2021): 1-13.

[5] Wu, Qiaoyun, et al. "Electroacupuncture alleviates neuropathic pain caused by SNL by promoting M2 microglia polarization through PD-L1." International Immunopharmacology 123 (2023): 110764.